CLAIMS

1. A Purified or isolated IL-7 conformer, wherein said conformer comprises the following three disulfide bridges: Cys: 1-4 (Cys2- Cys92); 2-5 (Cys34-Cys129) and 3-6 (Cys47- Cys141).

2. IL-7 conformer according to claim 1, wherein said IL-7 conformer is a recombinant human IL-7 conformer.

3. IL-7 conformer according to claim 2, wherein said IL-7 conformer comprises the amino acid sequence SEQ ID NO: 2 or 4.

4. IL-7 conformer according to claim 1, wherein said IL-7 conformer is a recombinant simian IL-7 conformer.

5. IL-7 conformer according to claim 4, wherein said IL-7 conformer comprises the amino acid sequence SEQ ID NO: 12.

6. IL-7 conformer according to anyone of claims 1 to 5, wherein said IL-7 conformer is not glycosylated.

7. IL-7 conformer according to anyone of claims 1 to 5, wherein said IL-7 conformer is glycosylated.

8. IL-7 conformer according to anyone of claims 1 to 7, wherein said IL-7 conformer is associated to the hepatocyte growth factor as a heterodimer.

9. IL-7 conformer according to anyone of claims 1 to 7, wherein said IL-7 conformer is functionally attached to a Fc portion of an IgG heavy chain through a peptide hinge region, said IgG being a human IgG1 or IgG4.

10. IL-7 conformer according to anyone of claims 1 to 7, wherein said IL-7 conformer is functionally associated to a Human Serum Albumin (HSA) or a portion of HSA as a fusion protein

11. An IL-7 drug substance comprising, as the desired product, an IL-7 conformer according to anyone of claims 1 to 9, said drug substance being substantially free of IL-7 molecular variants or product related impurities.

12. An IL-7 drug substance comprising, as the desired product, an IL-7 conformer according to anyone of claims 1 to 7, said drug substance being substantially free of IL-7 molecular variants or product related impurities, wherein the total amount by weight of IL-7 in said drug substance is at least 98% by weight, preferably at least 99.5% by weight.

13. A pharmaceutical composition comprising an effective amount of a drug substance according to claim 11 or 12 and one or more pharmaceutically compatible carriers.

14. Pharmaceutical composition according to claim 13, wherein the pharmaceutically compatible carrier is selected from sucrose, trehalose and an amino acid.

15. Pharmaceutical composition according to claim 14, wherein the pharmaceutically compatible carrier is contained in an appropriate buffer to form an isotonic solution.

16. Pharmaceutical composition according to any one of claims 13 to 15, wherein said appropriate buffer has a pH range comprised between 5 to 7.5, preferably 6 to 7, even more preferably of 6.5.

17. A pharmaceutical composition according to claim 16, wherein said appropriate buffer is an organic salt selected from a sodium citrate buffer and an ammonium acetate buffer.

18. A pharmaceutical composition according to claim 13, wherein said composition is a lyophilized form.

19. A pharmaceutical composition according to claim 13, wherein said composition comprises a protein (preferably human serum albumin) and/or a surfactant (preferably Tween 80).

20. A pharmaceutical composition according to anyone of claims 13 to 19, further comprising an immuno-stimulating agent selected from a hematopoietic cell growth factor, a cytokine, an antigen and an adjuvant, or a combination thereof, for combined, separate or sequential use.

21. A pharmaceutical composition according to claim 20, wherein said hematopoietic cell growth factor is selected from the Stem Cell Factor (SCF), particularly the soluble form of the SCF, G-CSF, GM-CSF, Flt-3 ligand, IL-15 and IL-2.

22. A pharmaceutical composition according to claim 20, wherein the cytokine is selected from γ interferon, IL-2, IL-12, RANTES, B7-1, MIP-2 and MIP-1α.

23. A pharmaceutical composition according to anyone of claims 20 to 22, wherein said antigen is selected from a synthetic or natural peptide, a recombinant protein, a killed, inactivated or attenuated pathogen product, a lipid, a portion thereof and a combination thereof.

24. A pharmaceutical composition according to claim 23, wherein said antigen is selected from antigens derived from HIV, Varicella Zoster virus, Influenza virus, Epstein Barr virus, type I or 2 Herpes Simplex virus, human cytomegalovirus, Dengue virus, Hepatite A, B, C or E virus, Syncytium respiratory virus, human papilloma virus, mycobacterium tuberculosis, Toxoplasma and Chlamydia.

25. A pharmaceutical composition according to anyone of claims 20 to 24, wherein said adjuvant is selected from any substance, mixture, solute or composition facilitating or increasing the immunogenicity of an antigen and able to induce a Th1-type immune response, such as CpG, QS21, ISCOM and monophosphoryl lipid A.

26. Pharmaceutical composition according to anyone of claims 13 to 25, for administration to a human patient for prophylactic or therapeutic stimulation of B or T lymphocyte development and proliferation, or for enhancement of global or specific immuno-reconstitution, or for enhancement of humoral or cellular immune response.

27. A pharmaceutical composition according to anyone of claims 13 to 25, to prevent or reduce opportunistic infections in immunodeficient patients.

28. A pharmaceutical composition according to anyone of claims 13 to 25, to prolong lymphopoiesis stimulation and/or to produce specific immune response and/or to broaden the repertoire of a specific immune response in human patients.

29. A pharmaceutical composition according to claim 26, 27 or 28, wherein human patients are immunodeficient patients, cancer patients, patients

undergoing grafts, patients infected with a virus or a parasite, elderly patients or any patients having low CD4 count.

30. A pharmaceutical composition according to anyone of claims 13 to 29, wherein the effective amount of the drug substance is comprised between about 3 to 300 µg/kg/day, preferably between 10 to 100 µg/kg/day, and in particular administered from once daily, to twice or three times a week down to once weekly.

31. A nucleic acid molecule encoding an IL-7 polypeptide, wherein said nucleic acid molecule comprises an altered Shine-Dalgarno-like sequence.

32. A nucleic acid molecule comprising a sequence selected from SEQ ID Nos: 1, 3, 12, 16, 18, 20 or 22.

33. A vector comprising a nucleic acid according to claim 31 or 32.

34. A recombinant host cell comprising a nucleic acid according to claim 31 or 32 or a vector according to claim 33.

35. A recombinant host cell according to claim 34, wherein said recombinant host cell is a human cell or a bacterial cell.

36. A recombinant host cell according to claim 35, which is *Escherichia coli* or *Bacillus Brevis*.

37. A recombinant host cell according to claim 35, which is a Chinese Hamster Ovary (CHO), HEK-293 cell line or a human stromal or epithelial cell line.

38.An antibody specifically immunoreactive with an IL-7 conformer as defined in anyone of claims 1 to 7.

39. A method of producing an IL-7 drug substance as defined in anyone of claims 11 and 12, the method comprising:

a) providing a sample comprising IL-7 polypeptides,

b) purifying an IL-7 conformer which comprises the following three disulfide bridges: Cys: 1-4 (Cys2- Cys92); 2-5 (Cys34- Cys129) and 3-6 (Cys47-Cys141) to produce an IL-7 drug substance, and

c) optionally, measuring or quantifying, in the drug substance, said particular IL-7 conformer.

40. The method of claim 39, wherein said sample is obtained from recombinant prokaryotic or eukaryotic host cells producing IL-7 polypeptides.

41. The method of claim 40, wherein said sample is (or derives from) a culture of prokaryotic host cells encoding an IL-7 polypeptide and further wherein the method further comprises, prior to step b):

i) treating said sample to cause a complete denaturation of said IL-7 polypeptides,

ii) optionally purifying the denatured polypeptide obtained in step i) and

iii) refolding the polypeptides.

42.The method of claim 41, wherein step i) comprises the dissolution of inclusion bodies in a denaturant buffer.

43.The method of claim 41 or 42, wherein step ii) is performed by hydrophobic chromatography, ion-exchange or inverse phase chromatography.

44. The method of claim 42, wherein said hydrophobic chromatography is implemented using HIC butyl.

45. The method of anyone of claims 41 to 44, wherein step ii) is carried out at a pH comprised between 6 and 9, preferably between 7 and 8,5 inclusive.

46. The method of anyone of claims 41 to 45, wherein said purification step b comprises the performance of an affinity chromatography.

47. The method of claim 46, wherein said affinity chromatography is performed on a column of sulfated polysaccharides.

48. The method of claim 47, wherein the sulfated polysaccharide is dextran sulfate or heparin.

49. The method of any one of claims 39 to 48, wherein the IL-7 conformer is characterized in the drug substance by Mass spectrometry, infra-red spectroscopy, NMR, by determining circular dichroïsm, by measuring the affinity toward a specific monoclonal antibody raised against said IL-7 conformer, or heparin affinity chromatography, and measured or quantified by ELISA, bioassay or the affinity of said IL-7 conformer for IL-7 receptor and any method of protein quantification if applied to the isolated conformer.

50. A method of controlling an IL-7-containing preparation, comprising determining the presence and/or relative quantity, in said preparation, of an IL-7 conformer as defined in any one of claims 1 to 9.

51. A method of producing an IL-7 drug substance or pharmaceutical composition, said method comprising (i) culturing a recombinant host cell encoding an IL-7 polypeptide, (ii) isolating said recombinant polypeptide to

produce an IL-7 drug substance and (iii) optionally, conditioning said IL-7 drug substance to produce a pharmaceutical composition suitable for therapeutic or vaccine use, said method further comprising a step of identifying, characterizing or measuring, in said drug substance or pharmaceutical composition, the quantity and/or quality of an IL-7 conformer as defined in any one of claims 1 to 9 and, more preferably, a step of selecting the drug substance or pharmaceutical composition which comprises, as the active ingredient, more than about 95%, preferably 98% of said IL-7 conformer.

52. A method according to claim 40 or 51, wherein IL-7 expression by the recombinant host cells is inducible, regulated or transient, so that the cell culture and IL-7 expression phases can be dissociated.

53. The method of claim 51 or 52, wherein the quantity and/or quality of said IL-7 conformer is determined by mass spectrometry-related methods, with or without tryptic digest, circular dichroism, NMR, specific monoclonal antibody analysis for disulfide bridges and/or conformation characterization.

54. Use of an IL-7 drug substance obtained by a method according to anyone of claims 39 to 49, for the manufacture of a pharmaceutical composition to induce a prolonged lymphopoiesis stimulation and/or to amplify an immune response.

55. Use of an IL-7 drug substance obtained by a method according to anyone of claims 39 to 49, for the manufacture of a pharmaceutical composition to prevent or treat a disease associated with an immunodeficiency.